Recommendations for Treatment as Prevention Among Heterosexual HIV Discordant Couples: A South African Case Study

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Abstract

The Human Immunodeficiency Virus (HIV) epidemic remains a major public health crisis even after thirty years of research. Despite great strides in the prevention and treatment of HIV-infected individuals, sexual transmissions continue worldwide and especially in sub-Saharan Africa (UNAIDS, 2013). Moreover, the increasing presence of heterosexual HIV discordant couples, where one partner in the couple is HIV-positive and the other is HIV-negative, presents unique challenges. Low perceptions of HIV risk and inadequate prevention strategies among this subpopulation fuel sexual transmissions. The WHO and UNAIDS recommend that targeted strategies be applied systematically which effectively treat the infected partner for his/her own health but also prevent HIV transmission to the uninfected partner (WHO, 2012). The proposed modality for accomplishing this task in this subpopulation is known as "treatment as prevention." The landmark HPTN 052 trial where the infected person received HIV antiretroviral therapy (ART) early in infection, which suppressed HIV and protected the infected person's immune system, but also reduced HIV transmission to the uninfected partner, confirmed this was as a promising method for reducing HIV incidence among discordant couples (Cohen et al., 2011). Harnessing information learned from discordant couples' studies, recommendations are presented as part of a comprehensive treatment as prevention program tailored to this subpopulation. These global recommendations include couples testing and counseling, condom education, education about and access to ART, and use of social marketing for implementation and optimal results. These recommendations are evaluated for their potential benefits in the context of a South African Case Study given South Africa's prominence in the HIV/AIDS epidemic, the significant presence of discordant couples and the South African government's commitment to HIV treatment and prevention efforts. Moreover, the South

African Case Study establishes the feasibility of the recommendations and helps to identify barriers that need to be overcome. Finally, a discussion of future research needed is presented for further optimization of the proposed treatment as prevention strategy.

Glossary of Terms

AIDS	Acquired Immunodeficiency Syndrome
ANC	Antenatal care
ART	Anti-retroviral therapy, A treatment for controlling HIV comprised of three or more anti-retroviral (ARV) drugs
ARV	Anti-retrovirals
CBO	Community based organization
CD4+ T cells	White blood cells that orchestrate immune responses; also known as T helper cells.
CHTC	Couples HIV testing and counseling
FBO	Faith based organization
HTC	HIV testing and counseling (focus on individual to be tested)
HIV	Human Immunodeficiency Virus
HIV Incidence	The rate of new HIV infections, usually measured as the rate of persons who become newly infected with HIV
HIV-Negative	A person who is not infected with HIV
HIV-Positive	A person infected with HIV
HIV Prevalence	The proportion of the population who are HIV positive at any given time point
HIV Serodiscordant Couple	A partnership whereby one partner in the couple is HIV-positive and one partner in the couple is HIV-negative; also known as “discordant couples”
Immune deficiency	Inability of immune system to work properly, resulting in susceptibility to disease
Immunosuppression	Immune system response to foreign invaders is reduced
Index Case	The HIV-infected partner in a serodiscordant couple
IPV	Intimate partner violence
PHDP	Positive health, dignity and prevention; a movement which encourages PLHIV to live healthy lives and prevent further HIV transmissions
PLHIV	People living with HIV/AIDS
PMTCT	Prevention of mother-to-child transmission of HIV
Replication	Process by which a virus makes copies of itself
VCT	Voluntary counseling and testing
Viral Load	A measure of the amount of HIV in the blood of an infected individual

Introduction

Human Immunodeficiency Virus (HIV), the virus that causes Acquired Immunodeficiency Syndrome (AIDS) in humans, remains an unresolved public health issue and the world's leading infectious killer with an estimated 36 million deaths since the epidemic began (World Health Organization [WHO], 2013b). Currently there are over 35 million people living with HIV/AIDS (PLHIV), indicative of the success of antiretroviral therapy (ART) in suppressing although not curing HIV, and slowing progression to AIDS. The ability to treat HIV infection is critical but stopping new infections to eliminate HIV remains a critical public health issue. Towards this end, in 2000 the United Nations acknowledged the critical need for an effective response to HIV/AIDS in the Millennium Declaration and set a target to reduce the sexual transmission of HIV by 50% by 2015 (UNAIDS, 2013). Although the HIV incidence rate decreased approximately 50% in 25 countries during 2001-2011 due to HIV prevention interventions, 2.5 million new infections occurred in 2011 alone (Cohen et al., 2013).

Moreover, it is estimated that 70% of all new infections occur disproportionately in sub-Saharan Africa; nearly 1 in every 20 adults in this geographic region are infected with HIV (UNAIDS, 2013; WHO, 2013b). One sub-Saharan Africa country, the Republic of South Africa, has experienced the greatest burden of HIV/AIDS with an estimated overall prevalence of 10%, and the largest population of PLHIV, and an estimated one out of every six PLHIV worldwide calling South Africa home (South African National AIDS Council [SANAC], 2011).

The WHO reports that there is increasing evidence that a substantial proportion of new HIV infections fueling the epidemic, both in sub-Saharan Africa and globally, occur within heterosexual, HIV serodiscordant couples, also described as "discordant couples" (2012). HIV discordant couples are defined as a partnership whereby one partner is HIV-positive and one

partner is HIV-negative (UNAIDS, 2013). Discordant couples represent a large subpopulation of PLHIV but have largely been under targeted in prevention and treatment efforts (Gay et al., 2012). In most sub-Saharan African countries, 75% of adults (aged 20-49 years) report being in stable cohabiting or married relationships, and for every PLHIV in a co-habiting couple, nearly half report a HIV-negative partner (WHO, 2012). Moreover, the majority of individuals in stable, cohabiting relationships do not know their own and/or their partner's HIV infection status or do not believe they are at risk for HIV infection. For those who do know their own and/or their partner's HIV infection status, they do not understand the concept of discordance and that they can prevent HIV transmission to their uninfected partner (WHO, 2012). UNAIDS emphasizes the critical need for discordant couples to be targeted with an effective HIV prevention strategy given the substantially increased risk for the uninfected partner to acquire HIV from his/her infected partner due to these reasons and the frequency of their sexual intercourse events (2013). The question remains how; what constitutes an effective, efficient and affordable intervention and how should an intervention be delivered to these couples in a way which encourages significant uptake and better health outcomes?

A potential solution for the subpopulation of heterosexual discordant couples is the concept of "treatment as prevention," a method of treating PHLIV with ART for HIV suppression, for the sake of their own health, but whereby they also receive extensive counseling and other behavioral interventions, to prevent HIV transmission to their uninfected partner (AVERT, 2014). This concept was demonstrated as a viable prevention modality among this subpopulation in the HIV Prevention Trial Network's landmark clinical trial as described below (Cohen et al., 2011). Although the findings are relatively new and additional research is needed, many in the HIV/AIDS field, including the WHO and UNAIDS, have put forth the concept of

treatment as prevention as a promising strategy for heterosexual, discordant couples in stable relationships. Critically, targeting this particular subpopulation affords an opportunity to increase HIV testing and counseling, support the infected partner's ART treatment and decrease HIV transmissions to the uninfected partner (WHO, 2012).

Goals of This Paper

To further explore this issue, this paper will present background information on HIV/AIDS, an overview of discordant couples and why many HIV prevention efforts are not reaching them and a review of the role of ART in treatment as prevention strategies. Recommendations for a proposed treatment as prevention approach among heterosexual discordant couples will be presented including targeted couples testing and counseling, condom education, education about and linkages to ART, and use of social marketing to be leveraged for optimal results. These recommendations will be examined in a general context but also specifically within the context of South Africa, which will be used as a case study given its prominence in the HIV/AIDS epidemic, the significant proportion of PLHIV in discordant relationships and the South African government's commitment to HIV prevention and treatment. The application of recommendations to the South African Case Study will be assessed to evaluate the potential benefits and potential barriers of this approach. Finally suggestions regarding future directions for research and practice will be presented.

HIV/AIDS

History of HIV/AIDS

The history of the HIV/AIDS epidemic is well documented in both scientific and public health literature. In the June 5, 1981 issue of the *Morbidity and Mortality Weekly Report (MMWR)* published by the Centers for Disease Control and Prevention (CDC) physicians

described the appearance of a mysterious, emerging infectious disease affecting previously healthy homosexual men in the United States. By 1982, the CDC had named the disease, which caused immunodeficiency, "AIDS" with documented cases expanding to also include heterosexual females, hemophiliacs, injection drug users, and Haitians (US DHHS, 2011). The landmark edition of the *MMWR*, and the case reports which followed over 30 year ago, are associated with the beginning of the HIV/AIDS epidemic we know today.

Biology & Transmission of HIV

HIV belongs to the virus family *Retroviridae* and the genus *Lentivirus* with lentiviruses being characterized by a substantial period between initial infection and observation of disease symptoms (National Institute of Allergy and Infectious Diseases [NIAID], 2012). HIV targets the host's CD4+ T cells; HIV utilizes the host cell's machinery to replicate with new virus particles released via budding through the host cell's membrane, which kills the CD4 cell. This replication cycle repeats over and over. Many of the antiretroviral drugs (ARV), which will be described later in further detail, work by disrupting this replication process (NIAID, 2012).

HIV spreads through body fluids and blood and is most commonly transmitted among adults via unprotected sexual intercourse with an infected person (CDC, 2013a). Although more rare, the virus can also be spread through oral sex (NIAID, 2012). Some HIV infections occur through contact with infected blood or equipment, e.g., sharing needles during intravenous drug use, accidental needle sticks in health care settings or infusion of contaminated blood with the latter being less likely in the developed world due to the advent of stringent screening processes. The most likely transmission route among HIV-infected children includes vertical transmission, either antenatal (before birth), perinatal (during birth) or postnatal (after birth), or during breastfeeding. HIV testing, counseling and ART are all key components for preventing mother-

to-child transmissions (PMTCT) (NIAID, 2012). Across transmission modes, evidence suggests the likelihood of transmission correlates positively with the concentration of HIV in the transmitting individual (Cohen & Gay, 2010).

Clinical Stages of HIV Infection

HIV infection can be characterized by three clinical phases termed acute infection, clinical latency, and AIDS. The acute infection period is defined as within two to four weeks post infection, whereby most individuals do not know they have been infected with HIV, but up to 70% experience flu-like symptoms due to the immune's system natural response to infection (NIAID, 2012). During this phase, large amounts of HIV particles are being produced and circulating in the blood, as measured by viral load. Likewise, large numbers of CD4+ T cells are being destroyed through this viral replication process (CDC, 2013a). The CD4+ T cells are a critical component of the host's immune system, so disruption of their function is devastating. It is during this period of high viral load that transmission risk is the highest. Towards the end of this phase, the immune system begins to decrease the amount of virus present and the CD4 cells begin to recover although not to the same pre-infection level (NIAID, 2012).

Following is the clinical latency period where HIV is active but reproducing at low levels. Phase duration varies depending on whether and when individuals initiate ART as described later in further detail. Critically, individuals are still able transmit HIV during this time (CDC, 2013a). Towards the end of this stage, untreated infected individuals simultaneously experience an increase in viral load and decline in CD4 cell count. The immune system weakens and individuals present with symptoms of HIV infection (WHO, 2013a).

In untreated individuals, the clinical latency period is followed by AIDS, the final stage of infection which is characterized by immunodeficiency and is defined by the occurrence of any

of more than 20 opportunistic infections, e.g., *Pneumocystis carinii* pneumonia (PCP), and a CD4 cell count ≤ 200 cells/µl of blood, as compared to 500-1,600 cells/µl observed in uninfected individuals (CDC, 2013a). Individuals with AIDS typically suffer from debilitating weight loss, infections of various organs and cancers, e.g., Kaposi's sarcoma. In the absence of treatment, individuals in this stage have a typical life expectancy of one to three years depending on the severity of their opportunistic infections (CDC, 2013a).

Heterosexual HIV-Serodiscordant Couples

As previously described, heterosexual discordant couples represent an important subpopulation contributing to new HIV infections and one that requires different prevention education and intervention strategies as those applied to individuals. Current data from sub-Saharan countries reveal that one-half to two-thirds of HIV-positive individuals in stable heterosexual relationships have an uninfected partner (Management Sciences for Health [MSH], 2012). As early as 2003, surveillance data indicated the majority of new HIV infections in sub-Saharan Africa were occurring between cohabiting couples (Allen et al., 2003).

One factor influencing these new infections is evidence suggesting the partners are unaware of their own HIV infection status, and if known, do not share this information with their respective partners. A 2008 study in South Africa revealed that men in long term partnerships rarely discuss HIV testing or infection status with their female partners, a finding which is common in many African countries. If their partner's status is known, often men assume their share the same HIV infection status or wait "to learn their status" until their female partner becomes pregnant and is tested for HIV during antenatal care (ANC) as part of PMTCT programs (Mindry et al., 2011). Even when the partners know he/she is infected, he/she is often reticent to disclose this information to their partner due to fear and the threat of stigma, discrimination, intimate partner violence (IPV) and relationship termination (MSH, 2012).

The HIV-infected partners within the discordant couples, termed index cases, comprise a large segment of the HIV-infected population, and the couples represent a subpopulation which should be targeted for HIV prevention interventions. However, the WHO reports the concept of "discordance" and the large presence of these couples are generally overlooked or poorly understood in many communities worldwide (2012). For this reason, discordant couples are often overlooked entirely or targeted with traditional HIV prevention strategies, which are successful for other subpopulations, but are largely ineffective among this subpopulation.

Traditional HIV prevention strategies focus on HIV testing, abstinence and/or consistent condom use, all of which tend to have low compliance among long-term, heterosexual couples given their predominant perception of low HIV risk (MGH, 2012). Medical male circumcision, a proven biomedical intervention for significantly reducing new HIV infections in males, has been widely promoted but does not directly address risk among females (WHO, 2012). One particular strategy, voluntary counseling and testing (VCT), or individual-initiated testing with counseling, has contributed significantly to increased HIV testing, condom use and reduced transmissions (Gay et al., 2012). However, this type of testing focuses on the individual and does not guarantee or support disclosure to the individual's partner. Moreover, concerns about IPV following disclosure in the absence of couples counseling make VCT sub-optimal (WHO, 2012).

When couples have been considered, HIV prevention efforts have focused primarily on encouraging elimination of males' use of sex workers and/or concurrent partners. Likewise, associated social marketing has been aimed at addressing issues of male domination of females and encouraging female empowerment to facilitate more open discussion about sex and HIV (Eyawo et al., 2010). These practices suggest there's an underlying assumption that the index case within the discordant couple is usually the male. However, research indicates that females

are equally as likely to be the index case in most countries (Eyawo et al., 2010). When the male is the index case, he often does not know he is infected; if he does know, his female partner may be overlooked for targeted HIV testing, counseling and treatment until she accesses health care during pregnancy, triggering a PMTCT intervention. Access to HIV prevention strategies at this point represents a missed upstream prevention opportunity (WHO, 2012).

For these reasons, this subpopulation of heterosexual discordant couples requires an approach for preventing HIV transmission between partners which differs from traditional approaches. In absence of consensus about the best way to target this subpopulation, there is general agreement that ART is a critical component of any solution (WHO, 2012).

ART a Major Treatment as Prevention Tool

What is ART?

As previously mentioned, HIV can be suppressed in infected individuals through the use of a combination antiretroviral therapy (ART) which is comprised of a "cocktail" of three or more antiretroviral (ARV) drugs (WHO, 2013a). The first ARV drug, zidovudine or AZT, was licensed by the US Food and Drug Administration (FDA) in March 1987; however, this treatment and others in the early years had problems with toxicity and adherence due to drug formulation, dosage, frequency and access issues (US DHHS, 2011). By 1996, companies had developed combination ART, and these drugs are divided into five classes based on how they target and disrupt the HIV replication life cycle (Johnson, 2012). As of 2012, there were 25 drugs available, with demonstrated reduced side effects and improved ease of use (CDC, 2013b).

World Health Organization's Guidelines on Initiation of ART

The 2010 WHO guidelines recommended that HIV-positive adults initiate ART once their CD4 counts reach ≤ 350 cells/μl (2013a). However, in 2013 the guidelines were revised to

recommend ART initiation at a higher CD4 level (≤ 500 cells/µl). This revision is due to a recent study, as described later, which demonstrated that earlier initiation of ART by HIV-infected individuals is beneficial for their own health. Beyond the health benefits to the HIV-infected individual, this same study also demonstrated that ART treatment of the infected individual reduced the risk of transmitting HIV to his/her partner. For this reason, the 2013 WHO guidelines now recommends ART for HIV-positive individuals in discordant relationships, regardless of their CD4 level (2013a). Finally, the 2013 guidelines recommend ART, regardless of CD4 count, to HIV-positive children under five years, HIV-positive pregnant or breastfeeding females, and all HIV-positive individuals with active tuberculosis or hepatitis B (2013a).

How Does ART Work as Treatment in HIV-Infected Individuals?

When utilized as directed, ART is a highly efficacious method for treating HIV-infected individuals which protects their health and delays onset of AIDS. ART suppresses but does not eliminate HIV by interfering with HIV replication, thus decreasing the virus concentration in the blood (viral load) and genital secretions. Early initiation of ART results in a reduced latent viral reservoir, meaning there is less virus present in the infected individual as compared to someone who initiates ART at a lower CD4 count (Cohen et al., 2013). This significant reduction in viral load preserves the CD4 cells and their immune function, thereby safeguarding of the immune system to fight ordinary infections (NIAID, 2012).

Prior to the advent of ART in the mid-1990's, individuals often progressed to AIDS within a few years; today, infected individuals who initiate ART early and receive proper medical care can control the virus and experience a prolonged and often near normal life expectancy (CDC, 2013a). Moreover, ART treatment of PLHIV reduces the amount of virus circulating in the population which reduces HIV incidence rates. UNAIDS estimates 6.6 million

AIDS-related deaths worldwide have been averted due to ART (2013). Despite these advantages, ART as an effective treatment of HIV-infected individuals requires that people know their HIV infection status, strictly adhere to their regimen and maintain access to health care.

ART Treatment as Prevention of HIV

In the absence of a vaccine and the inability of behavioral modifications to eliminate HIV transmission, HIV/AIDS researchers and practitioners began investigating whether the aforementioned benefits of ART for individuals could be translated into a potential preventative tool against sexual transmission of HIV to others (WHO, 2012). The CDC defines this concept, known as treatment as prevention, as "a strategy for treating HIV-infected persons to improve their health and to reduce the risk of onward transmission" (2013b, pg. 1). The treatment as prevention concept is not a new practice; it has been in wide use since the mid-1990's but aimed at pregnant women to prevent HIV transmission to their children during pregnancy and breastfeeding (AVERT, 2013). Discordant couples comprise a specific subpopulation which could clearly benefit from such a strategy.

Evidence from several studies supports that transmission risk increases as viral load increases (Cohen & Gay, 2010). Observational data, ecological studies and modeling suggested decreased transmission of HIV from infected partners on ART to their uninfected partners but definitive proof was lacking (Cohen et al., 2011; Anglemyer et al., 2011). However, it was the landmark HPTN 052 trial, as described below, which galvanized treatment as prevention as a relevant strategy for preventing heterosexual transmissions within discordant couples.

The HPTN initiated this randomized, controlled clinical trial termed "052" in 2005, which included 1,763 discordant couples in stable, heterosexual relationships, across 13 sites in nine countries including South Africa. The study hypothesized whether ART, proven to reduce

viral replication, could limit HIV transmission within these discordant couples (Cohen et al., 2011). Moreover, the trial compared early versus delayed initiation of ART for HIV-infected participants. All study participants were part of a discordant couple with the HIV infected individuals having CD4 counts between 350-550 cells/μl and no history of ART (with the exception of short-term use for PMTCT). The study protocol employed a randomization scheme to assign half of the HIV-infected participants to the early-therapy group for immediate initiation of ART at enrollment. The other half of HIV-infected participants were assigned to the delayed-therapy group where their treatment was delayed until their CD4 counts were < 250 cells/μl or they developed an AIDS-related illness (Cohen et al., 2011). Following enrollment, trial participants attended three monthly visits, followed by quarterly visits. During these visits, the participants and their partners received joint counseling regarding HIV education, risk reduction, condom usage, STI treatment and management of other medical conditions. The uninfected partners were tested for HIV on a quarterly basis. The primary prevention endpoint was linked HIV transmission in uninfected partners, meaning that if a transmission occurred, clinicians could confirm the index case in the couple transmitted their virus to the previously uninfected partner using comparative sequence analysis techniques (Cohen et al., 2011).

The HPTN 052 trial is scheduled for completion in 2015 with original plans to compare the groups at that time. However, in April 2011 an independent monitoring board for the trial recommended that the trial results be made public; the trial had demonstrated that if an HIV-infected partner in a heterosexual, discordant couple was counseled and adhered to an effective ART regimen early in infection, there was observed suppression of HIV viral levels in the genital tract of the infected partner (Cohen et al., 2011). Consequently the risk of sexually transmitting the virus to their uninfected partner was reduced by 96%. In total, 39 transmissions were

observed and 28 were virologically linked meaning the viral sequence in both the index case and newly infected partner were almost identical. Notably, of these 28 linked transmissions, only one transmission event was observed in the early treatment arm suggesting the early initiation with ART contributed to the observed decrease in transmission risk. Finally, 11 of the transmission events were not virologically linked meaning that the index case in the couple did not infect their previously uninfected partner, but rather that the newly infected partner acquired HIV through someone external to the relationship (Cohen et al., 2011). The implications of this latter finding suggest that in addition to ART therapy, there remains a critical need for education and counseling regarding risk reduction behaviors, such as discouraging multiple sexual partners and using safe sex practices, for the prevention of HIV infection.

The results of this trial demonstrated that ART as treatment as prevention, in this specific subpopulation of heterosexual discordant couples, along with couples counseling and HIV education, was efficacious for drastically reducing HIV transmissions. *Science*, one of the world's leading scientific journals, named the HPTN 052 as "Breakthrough of the Year" and many called the results a complete "game changer" due to the nearly 100% efficacy observed (Cohen, 2011). Prior to proving treatment as prevention worked in this subpopulation, the primarily emphasis of ART treatment focused on benefits to the HIV-infected individual rather than the additional benefit of preventing transmission to the uninfected partner. As previously described, the results also prompted the WHO to revise their guidelines to include earlier initiation of ART by HIV-infected individuals for their own health, but also initiation of ART by HIV-infected individuals in discordant relationships to provide potential protection from HIV transmission to their uninfected partner. Finally, in 2012 the WHO also issued a set of guidelines addressing treatment as prevention in discordant couples (2012).

Access to ART Globally

A critical component of any ART treatment strategy is access to ART. This is true for treatment of individuals and for treatment as prevention strategies for discordant couples. These drugs are so vital in the battle against HIV that in 2000 the United Nations set a Millennium Development Goal to provide ART to 15 million PLHIV by 2015 (UNAIDS, 2013). In 2012, more than 9.7 million PLHIV in low and middle income countries received ART (WHO, 2013b). These statistics represent a nearly 30-fold increase in the number of people receiving ART in developing countries during 2003-2012, and close to a 20% increase during 2011-2012 alone. However, key issues regarding access and affordability of ART remain and need to be addressed. As of 2010, it was estimated that for every one PLHIV receiving treatment, another four PLHIV need it (Cohen & Gay, 2010). Under the new 2013 guidelines, an estimated 29 million PLHIV were eligible to initiate ART, indicating only 34% of now eligible PLHIV were receiving ART. Continued rapid scale up is needed to ensure adequate coverage (UNAIDS, 2013).

Recommendations

The review presented in the previous section outlines why heterosexual discordant couples constitute an important subpopulation in urgent need of targeted HIV treatment as prevention strategies to benefit both the infected and uninfected individuals in the partnership. The recommendations which follow aim to address the previously described factors which contribute to transmission risk between the partners. In summary, these factors include:

- *Lack of knowledge regarding HIV infection status*
- *Unwillingness to disclose HIV infection status*
- *Poor or no understanding about discordance*
- *High frequency of sexual intercourse events within discordant couples*

- *Absence of and/or inconsistent condom usage*
- *Lack of knowledge, access and adherence to ART for the index case*
- *General stigma, fear and lack of support to address HIV within their relationships*

The following recommendations also seek to provide appropriate channels and mechanisms for this subpopulation to receive the proposed treatment as prevention intervention in a way that is relevant and tailored to them. Finally, these recommendations should be implemented as a comprehensive treatment as prevention program for optimal results.

1. ***Increased Access to Couples HIV Testing & Counseling (CHTC) with Support for Mutual Disclosure and Education Regarding Discordance***

Global consensus remains that access to knowledge of HIV infection status through testing and counseling methods is critical to expanding access to treatment, support and information and to prevent further transmissions (Gay et al., 2012). CHTC provides an opportunity for couples to receive condoms, information on HIV and discordance, understand their risk, to test and share their status with one another in a guided and safer environment, and learn how condoms and ART can be utilized to treat HIV and prevent transmission within their relationship (Kelley et al., 2011). All CHTC regardless of setting should provide linkages to access to ART for discordant couples (Kennedy et al., 2011). Moreover, CHTC is the central entry point for accessing the collective set of recommendations delivered as an intervention package and facilitates adherence to the intervention. Finally, the WHO recognizes the critical role of CHTC in treatment as prevention interventions for discordant couple and developed guidance on the best methods for delivering it (2012).

2. ***Increased Access, Education and Emphasis on Condom Usage for Long Term Couples***

USAID indicates that programs which promote correct condom usage are integral to any effective HIV program (2013b). This recommendation is critical given research suggests that

long term heterosexual couples are less likely to use condoms due to their perceived low risk for HIV. Messaging about consistent condom usage among long term couples and in the context of discordance is needed (Kennedy et al., 2010). Studies report condom use among discordant couples increased following effective CHTC (Kennedy et al., 2010; Allen et al., 2003).

3. Increased Access to ART for Discordant Couples in Accordance to 2013 WHO Guidelines

The "game changing" results from HPTN 052 and revised WHO guidelines leave no doubt that ART as treatment as prevention in discordant couples is strongly advisable for the health and stability of the individuals in the couple unit (WHO, 2012). It is critical that discordant couples have access to ART to prevent new transmissions. Many countries have made great strides to ensure that HIV-infected individuals have access to ART. However, with the previously described revisions to the WHO guidelines, more PLHIV will need access to ART. The WHO has indicated that in cases where both HIV-infected individuals and discordant couples both meet the guidelines for ART initiation but supply shortages exist, HIV-infected individuals should be given priority access (2012). In addition to price and supply related access issues, the index cases in discordant couples need to be able to access clinics where they can continue to maintain access to ART and be monitored sufficiently for optimal adherence to the prescribed regimen (WHO, 2012). Finally, it should be noted that some studies have indicated that ART may be advisable for the HIV-negative partner as well, but for the purposes of this review, the provision of ART will be specific to the HIV-infected partner.

4. Increased Education Regarding ART and Promotion of Treatment as Prevention for Discordant Couples

Discordant couples also should be thoroughly educated on ART's HIV prevention power and what the concept of treatment as prevention entails; specifically, the infected partner's strict

adherence to the prescribed ART regimen, faithfulness and safe sex practices between the couple and continued treatment and monitoring of the infected partner and HIV testing for the uninfected partner (WHO, 2012).

5. Utilization of Social Marketing for Enhancing Implementation of Recommendations

A final recommendation is to utilize social marketing for facilitating acceptance, delivery, and compliance to a treatment as prevention program. Social marketing is a collective set of strategies which can be applied to enhance public health interventions. Kotler & Zaltman define social marketing as "the design, implementation, and control of programs calculated to influence the acceptability of social ideas and involving considerations of product planning, pricing, communication, distribution, and marketing research" (1971, pg. 5). Engaging in social marketing activities facilitates enhanced understanding of target audiences including their environments, values, beliefs and constraints. Once these elements are understood, programs can apply social marketing, which harnesses the four classic commercial marketing strategies of product, price, place and promotion and combine them in a synergistic way to encourage adoption of this desired behavior by reducing barriers, increasing benefits and utilizing facilitators (Newton-Ward, 2013b). For example, the increased sales and reported utilization of condoms marketed for the prevention of HIV in sub-Saharan Africa is a well-documented example of the power of social marketing (Sweat et al., 2012).

While critical to the implementation of a successful treatment as prevention program, a complete social marketing plan is beyond the scope of this paper. The specific details of how to perform social marketing are complex and require extensive research and associated financial support. However, a brief outline of proposed social marketing strategies applied in the context of the South African Case Study, as described below, is presented in the Appendix.

A South African Case Study for Translating Recommendations into Practice

The collective recommendations for a comprehensive treatment as prevention strategy for heterosexual discordant couples presented here are relevant to many global settings. However, since the recommendations are fairly broad, there will be challenges implementing them worldwide on a large scale due to logistical and financial obstacles and the recommendations may be more readily implemented in specific countries. Moreover, the inclusion of social marketing strategies dictates a tailored approach. For these reasons, it is advantageous to discuss the application of these recommendations, such as anticipated benefits and barriers, using a specific country as a case study as well as for considering how social marketing can highlight benefits and reduce barriers to facilitate compliance as presented in the appendix. For this purpose, the Republic of South Africa is presented as a case study given its predominant role in the HIV/AIDS epidemic, a large presence of discordant couples, and the government's demonstrated leadership and commitment to HIV prevention and treatment efforts.

South Africa remains one of the hardest hit countries in the global HIV/AIDS epidemic. South Africa has approximately 5.26 million PLHIV among its population of approximately 53 million people (Statistics South Africa [Stats SA], 2013). The size and nature of the South African HIV epidemic make addressing this public health issue a daunting but necessary challenge. Estimates suggest only 25% of South Africans have had a HIV test (CDC, 2012). However, estimates in 2009 indicated that over 1,000 South Africans are infected with HIV each day, with the majority occurring via sexual transmission (SANAC, 2011).

South Africa's commitment and successful efforts during the last decade to expand access to HIV prevention and treatment services, including ART, make it an ideal case study for implementation of the treatment as prevention strategy. The South African government leads a

universal HIV treatment program, which is administered through the public health system with new policies and infrastructure to offer HIV testing and services at local health clinics, making access to a variety of services and ART more feasible (Beaubian, 2013). This highly coordinated and systematic approach to treating HIV is critical given estimates that 15.9% of the adult population aged 15-49 years is HIV-positive (Stats SA, 2013).

UNAIDS reports that South Africa leads the world in expanding access to ART with greater than 80% of eligible adults receiving ART in 2012, indicative of a 27% increase in provision as compared to 2011 (UNAIDS, 2013). In South Africa, ART access issues related to price should not be an issue given the government provides ART to nearly 2.15 million PLHIV every day for free or very low cost due to price negotiations, subsidies and donations (Beaubian, 2013). South Africa purchased $700M (USD) worth of fixed-dose ART regimens in 2012, reflecting a nearly 38% price reduction, as part of its long-term sustainability plan (UNAIDS, 2013). As a result of commitment to treat PHLIV in areas with high HIV incidence and prevalence, such as the KwaZulu-Natal province of South Africa, life expectancy increased by 11.3 years between 2003-2011 following the ART scale-up in 2003 (Tanser et al., 2013). Clearly, South Africa serves as a model for addressing the price, supply and distribution dimensions of ART access. However, a challenging dimension of ART access remains; how to balance the prioritization of ART for infected individuals meeting CD4 count requirements versus those infected individuals who are part of discordant couples.

South Africa is also a relevant country for studying discordant couples and implementing strategies aimed specifically at this subpopulation. In 2011, the South African government estimated the presence of at least 817,000 discordant couples (SANAC, 2011). South Africa, like many other African countries, experiences low marriage and cohabitation rates, and later age of

marriage; these factors influence the acceptability of multiple and concurrent sexual partners, and contributes to the increasing number of discordant couples. Moreover, with a large migrant population, often couples are separated for long periods of time which also significantly contributes to additional partners including transactional sex, new sexual transmissions and increasing discordancy (SANAC, 2011). Although these two issues may be more prevalent in South Africa as compared to other global settings, these issues are still relevant and must be addressed in treatment as prevention strategies for the couples.

The previously presented issues facing discordant couples in other global settings, including their perceptions of low HIV risk and inadequate HIV prevention efforts, are also relevant to discordant couples in South Africa. Condom use remains relatively low among long term couples in general and females are equally as likely as males to be the index case in heterosexual discordant couples South Africa (SANAC, 2011). However, in terms of risk behaviors, studies in South Africa suggest that access to ART with increased testing and counseling results in behavior modifications to minimize HIV transmission risk among discordant couples (Johnson et al., 2012). Based on the large presence of discordant couples, South Africa has already initiated implementation of some CHTC on a limited basis and is investigating solutions to overcome barriers (Dilmitis, 2011; CDC, 2012).

Finally, social marketing strategies have been utilized widely and effectively in South Africa for other HIV prevention modalities such as general HIV education, condom and lubricant usage, male circumcision, VCT and PMTCT to enable behavior modifications, all of which have been critical in decreasing HIV transmission rates (Johnson et al., 2012; Population Services International [PSI], 2013). In order to increase compliance, discordant couples need to believe in the benefits of adhering to these treatment as prevention components, which include remaining

monogamous, consistently using condoms, receiving care, testing and counseling and using ART, protects their own health and drastically reduces risk their chances of HIV transmission to their uninfected partner (Smith et al., 2012). Issues with compliance to these strategies can be addressed using social marketing strategies to identify and overcome the root cause of these barriers (Newton-Ward, 2013a). This latter exercise is better facilitated in South Africa where social marketing for HIV prevention and treatment strategies are already widely in use.

Discussion

Benefits Associated with Treatment as Prevention Recommendations

The benefits associated with the collective treatment as prevention recommendations are numerous. The packaged message for discordant couples is that the treatment as prevention strategy among heterosexual discordant couples affords a life changing opportunity to avert transmissions if applied in the context of routine couples-based testing, counseling and support, safe intercourse practices, and adherence to ART regimens (CDC, 2013b). Once again, using South Africa as a case study provides a specific setting to assess these benefits. The literature indicates that many of these couples in South Africa do not know their individual HIV infection status or assume they share the same status and perceive their HIV risk is low risk given the nature of their relationship status; these couples do not see the utility of condoms for these same reasons and view HTC as an individual activity. These couples likely do not realize that effective ART treatment of the infected partner not only safeguards his/her health but also can prevent further transmission to his/her uninfected partner (WHO, 2012). For these reasons, it is critical to emphasize the benefits of adherence to these collective recommendations and convince couples that their participation is beneficial and necessary for their long term health and life stability.

CHTC is especially beneficial as it serves as an upstream intervention with many promising downstream behaviors which predict better health outcomes for both partners. South Africa acknowledges the powerful impact of CHTC and has engaged celebrity couples in marketing CHTC (SANAC, 2011). Effective CHTC by trained providers can positively influence the couples, regardless of marital status, by increasing partner cohesion and decreasing the threat and/or presence of IPV which can drive fear of testing and of sharing results (Gay et al., 2012). Data reveals more women than men are tested, thus resulting in women disparately bearing the burden of disclosure. More men testing via CHTC helps increase men's knowledge of HIV, mitigates some IPV concerns and helps establish new social norms (Dilmitis, 2011). Published studies, including those in South Africa, suggest that once individuals learn their infection status and receive counseling, they are more likely to adopt preventive behaviors as compared to individuals who do not know their status (WHO, 2012). In addition, effective CHTC facilitates access to care and encourages early initiation and adherence to ART by the infected partner, improving that partner's own health via decreased viral load and risk for drug resistance, preservation of CD4 cells and delayed onset of AIDS (Wong, 2013).

Collectively, these treatment as prevention recommendations provides an opportunity for the HIV-positive partner to play a prominent role in prevention efforts, a critical component of the "positive health, dignity and prevention" movement (MSH, 2012). This intervention affords an opportunity for both safer family planning and conception and reductions in HIV incidence in infants (WHO, 2012). Several studies suggest that discordant couples are receptive to this information but healthcare workers do not routinely engage them in this discussion if not specifically asked (Matthews et al., 2012). CHTC can also serve as a decision point regarding male circumcision, another evidence based HIV prevention strategy (WHO, 2012). Notably, the

counseling portion of CHTC is especially critical; it serves as a channel for receiving quality education about HIV, support for PLHIV and decreasing stigma associated with HIV/AIDS within the partnership, their families and communities and (WHO, 2012).

The benefits associated with condoms are well known as they are an efficient and affordable evidence based method for preventing sexual transmission of HIV (USAID, 2013b). South Africa has experienced great success with social marketing for increased usage of male condoms. Modeling suggests condoms contributed significantly to lower incidence rates observed during 2000-2008 (WHO, 2012). It is hoped that similar declines will be observed among discordant couples. A study in South Africa exploring contraception practices of HIV-positive females on ART found they were more likely to utilize condoms if they knew their partners were uninfected, another promising benefit of these recommendations (Oni et al., 2013).

Targeting heterosexual discordant couples with these recommendations may also provide enhanced opportunities for HIV-infected men to access ART. Data from sub-Saharan Africa in 2012 suggested HIV treatment coverage for eligible males (57%) is much lower as compared to eligible females (73%), likely due to the large amount of HIV testing and treatment efforts focused on PMTCT (WHO, 2012). Ideally, targeting couples will result in more males being tested and initiating ART earlier. Moreover, more men being diagnosed and treated also drive down stigma which cripples women's roles in prevention efforts (Gay et al., 2012).

If the proposed treatment as prevention strategy is successful, a substantial number of new infections within this subpopulation could be averted. Among heterosexual discordant couples in South Africa, the literature reports an incidence rate of 1.48 transmissions per partner per 100 person-years, for individuals without suppression of HIV (Walensky et al., 2013). As previously described, the South African government estimated the presence of at least 817,000

discordant couples in 2011. In the absence of viral suppression in the index case, it's reasonable to expect an estimated 12,092 linked transmissions in a given year. However, assuming the treatment as prevention strategy described here is as successful as the results observed in HPTN 052, there's potential to observe up to a 96% relative reduction in linked transmissions among this subpopulation (Cohen et al., 2011). If the 96% relative reduction in linked transmissions is applied to discordant couple subpopulation in South Africa, there's the potential for averting 11,608 linked transmissions in a given year. This estimate is for one year only such that over time more infections could be averted. Finally, this estimate assumes that the 96% relative reduction in linked transmissions observed in HPTN 052, which included multiple countries, can be translated from the clinical to a non-clinical setting specifically in South Africa.

Moreover, the Cost-Effectiveness of Preventing AIDS Complications International Group's analysis, designed to mirror the HPTN 052, suggests long term cost savings due to ART in South African discordant couples (Walensky et al., 2013). The five year survival rate among index cases increased to 93% with early initiation of ART, thus preventing opportunistic infections such as tuberculosis, the cause of death in 50% of all HIV-infected people (Walensky et al., 2013). Within five years, models suggest South Africa could experience cost savings via early initiation of ART in discordant couples as they stayed uninfected or healthier (Walensky et al., 2013). Economic analysis suggests that investment in services, such as those proposed, yield economic returns up to three times greater due to increased employment and productivity and averted or deferred future expenses for medical services and orphan care (WHO, 2012).

Barriers to Implementation of Treatment as Prevention Recommendations

Although this set of recommendations is well-founded, discordant couples in South Africa and worldwide face barriers which could potentially discourage or prevent optimal

uptake. Several studies cite the most significant barrier preventing discordant couples from accessing testing and counseling is their perception of low HIV infection risk and a lack of knowledge about discordance (Gay et al., 2012). These recommendations are underpinned by the need for individuals to know their HIV infection status as early as possible, which as previously described, prompted the WHO to recommend that infected individuals with discordant partners should initiate ART regardless of their CD4 count. Access to general testing or the specific HIV test needed during acute infection can be challenging (Cohen & Gay, 2010).

The concept of CHTC has been studied in many African countries and found to be an effective testing and counseling modality. However, estimates indicate less than 1% of couples used this joint service (Kelley et al., 2011). As previously discussed, many partners do not seem to understand the utility of CHTC given their perception that their infection status is the same or lack of knowing they can prevent transmissions within their partnership (Kelley et al., 2011). Barriers can be simple, e.g., lack of knowledge that CHTC services are available, or can be quite complicated. Studies reveal that partners are reticent to suggest couples testing due to fear of what the suggestion may imply or their partner's reaction to a positive test result. This perception can be further exacerbated by relationship insecurity and challenges of maintaining long term relationships, both predominant issues within South Africa (Mindry et al., 2011).

Barriers to accessing testing and counseling appear to be different among the female and male partners. The cited barriers for women generally include lack of time, monetary resources, transportation and childcare services to access services or lack of information that testing is necessary for them (Gay et al., 2012). Research indicates many women do not undergo testing due to fear of anticipated reactions following disclosure, which quite often includes abuse, moral judgment, relationship termination, discrimination and ostracism. Fear of IPV is a real concern in

South Africa where levels of gender-based violence are very high and often part of normal culture (Harrison et al., 2006). Studies document that females are often expected to initiate HIV-related discussions despite their low negotiating power (Mindry et al., 2011). Studies indicate men often cite inconvenient hours of operation or location as reasons for not submitting to HIV testing and counseling. Men also tend to not access HTC via health services as they may not use health services at all for various reasons (Katz et al., 2009).

Specific to couples testing, men often fear testing and disclosure of status to their long term partner if they already believe or know they are infected. Furthermore, men often fear they may have been infected due to short term affairs, with partners outside of their long term relationship (Gay et al., 2012). CHTC may be challenging given the physical separation of couples when one partner is a migrant worker or simply because they often are not married or cohabiting. CHTC is also more expensive and labor intensive than individual testing and studies of PMTCT have demonstrated that engagement of males can be difficult although male participation provides significant value added (SANAC, 2011).

Another potential barrier is concern about increased sexual risk once couples realize ART decreases transmission risk. Some studies suggest individuals on ART are more likely to engage in riskier sexual behavior if they perceive their treatment prevents transmission (Cohen & Gay, 2010). In contrast, other studies including one in South Africa, reported reductions in sexual risk behaviors after ART initiation, due in part to consistent prevention messaging. However, it is unclear if findings among individuals are relevant to discordant couples. Many clinicians suggest that perhaps these misconceptions and risks can be mitigated through long term clinical care and counseling of couples with an emphasis on safe sex practices (Venkatesh et al., 2011).

Future Directions for Research and Practice

The recommendations set forth are based on studies among stable, heterosexual discordant couples which support ART as treatment as prevention among this subpopulation. However, questions remain if the treatment as prevention strategy will be efficacious in the subpopulation discussed here due to multiple components which seem to be required. Currently, it is unknown how significantly each component, e.g., CHTC, condom use, ART, and education, contributes to a successful treatment as prevention strategy; specifically, what is the expected outcome if one or more components are missing (Cohen et al., 2013).

Another more general question is whether or not the success observed in the controlled studies will translate into real world settings. This is an important question that is applicable to many new scientific breakthroughs and is being discussed in the implementation science literature but is beyond the scope of this paper to resolve (Bhattacharyya et al., 2009).

Beyond these questions, future studies are needed on ART as a key component of treatment as prevention strategies. Although studies conclusively support that ART suppresses HIV, there is evidence that HIV suppression in the genital tract is incomplete; research indicates some individual components of ART do not penetrate genital secretions at all. Moreover, it is well documented that some individuals experience ARV drug resistance so the correct formulation, combination and strict adherence of ART is needed to ensure optimal performance of ART in treatment as prevention strategies (Cohen & Gay, 2010). Long term studies are needed to assess the impact of ART on HIV-infected individuals, the durability of their own drug induced HIV suppression, and the durability of protection against transmission within the context of modulating risk behaviors due to changes in risk perception over time (Anglemyer et al., 2011). All these concerns will require frequent monitoring and counseling with the couples

(Cohen et al., 2013). Finally, it should be noted that some studies have indicated that ART may be advisable also for the HIV-negative partner, as a form of pre-exposure prophylaxis. This option should be further considered for greater efficacy and compared to value added in the context of ART cost and access issues (WHO, 2012).

Other future considerations include how generalizable the findings of these studies will be among other subpopulations, e.g., less stable discordant couples and MSM (Cohen et al., 2013). Beyond benefiting people on an individual or partnership level, future studies, such as the HPTN 071 trial being conducted in South Africa and Zambia, are needed to demonstrate ART's utility as treatment as prevention on a population level (Smith et al., 2012). If results suggest this strategy is more relevant for specific subpopulation or within the context of specific environments, this could impact the roll out of these types of strategies including funding and access to ART given how many PLHIV need it (Cohen et al., 2013). Likewise, another new prevention strategy with possible potential is universal testing and treatment using ART. Although considered controversial, various modeling scenarios have suggested HIV can be eliminated in countries such as South Africa within a varying number of years by initiating annual HIV screening, initiating ART, and assuming a set uptake (Hontelez et al., 2013). This model negates the highly influential component of counseling so many opponents do not support this strategy. Although it seems likely that this strategy will not be suitable for discordant couples due to the absence of counseling, it should be considered (Gay et al., 2012).

Another future area for additional research is reaching couples where one partner does know their HIV infection status and intentionally does not share it for the previously described reasons. Reaching these couples and getting them into CHTC is critical but will be especially challenging. Since the mainstream social marketing, which is aimed at couples who do not know

their HIV infection status, may be irrelevant for this group, additional research will be needed to determine how to best reach this important subpopulation. Another area for continued research linked to counseling is the continued long term support for couples. It should not be assumed that the same support system used to support individuals will be adequate for supporting couples. There are many cultural and socioeconomic factors influencing the couples in their daily lives but also in how they navigate life living with HIV.

Conclusion

In the 33 years since the first reported case of AIDS in the US, a diagnosis of HIV infection has transitioned from a death sentence to a more manageable chronic disease when infected individuals are able to access health care and ART (US DHHS, 2011). However, despite these improvements, HIV remains at epidemic proportions across much of the world, disparately affecting populations and disrupting families and socioeconomic functions, and remains cloaked in fear and stigma. Moreover, this paper highlights the fact that heterosexual transmissions are fueling new infections globally, including the large presence of discordant couples, and the fact that traditional prevention modalities may not be sufficient. Therefore, it is essential that countries address this under targeted subpopulation with effective prevention modalities.

The paper presents a collective treatment as prevention approach which begins with increased access and promotion of CHTC, a focal point for the identification of discordant couples through HIV testing with support for mutual disclosure of test results. During CHTC, both partners can receive education about the concept of discordancy, and how ART can be used not only to treat the infected partner for the sake of his/her own health but also to prevent transmission to the uninfected partner. During the CHTC, discordant couples can also receive education about HIV, prevention efforts, and safe sex practices such as consistent condom usage.

In this treatment as prevention approach, discordant couples need increased access and linkages to ART including routine monitoring of the index cases for optimal adherence to their ART regimen. Finally, this collective treatment of prevention approach dictates that each component be implemented, i.e., simply increasing access to ART is not enough. To fully realize the prevention benefits evidenced in recent studies, ART for infected partners should be coupled with CHTC, prevention education and condoms as previously described. Moreover, social marketing can be harnessed as a strategy to improve delivery of an implemented treatment as prevention program, given social marketing's proven reputation for enhancing delivery of public health interventions, to improve health outcomes and eventually turn the tide on new HIV infections (Newton-Ward, 2013a). Areas for future research have been identified which would also facilitate enhanced implementation of the proposed recommendations.

These recommendations presented are globally relevant but were discussed in the context of a South African Case Study for greater clarity and more manageable application. South Africa serves as an ideal environment for treatment as prevention program focused on heterosexual discordant couples. Narrowing the focus of such a complex set of recommendations affords an opportunity to critically consider the associated benefits and barriers to such a plan on a smaller scale. Following evaluation and application of lessons learned, these recommendations could be tailored to discordant couples in different geographic areas as well as to different subpopulations.

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Appendix

Outline of Proposed Application of Social Marketing Strategies for Implementation of Recommendations in South Africa

An preliminary outline of proposed marketing components including product, price, place and promotion offerings is presented below which can be applied as a first step to create facilitators which make adoption of the suggested behavior, i.e., participation in a comprehensive treatment as prevention program, seem necessary, reasonable, easy, and acceptable to heterosexual discordant couples (Newton-Ward, 2013a).

Product Marketing Strategy

Many discordant couples do not engage in HIV testing, use condoms or ART as prevention due to low perceptions of risk for HIV transmission or they assume they share the same HIV infection status, thus making the product marketing strategy critical. Lee & Kotler describe the product or service as "a mechanism that enables the target audience to translate their motivation into action" (2011, pg. 248). For the proposed treatment as prevention program, the core service is the CHTC, where couples receive education, counseling and testing for HIV and learn how to minimize HIV transmission using the core products of condoms and access to ART. Once educated and motivated, these products and services, along with the other marketing components, give discordant couples control to treat and prevent HIV, and safeguard their health.

Price Marketing Strategy

Price is defined as "the cost that the targeted audience associates with adopting the desired behavior" and the cost can be both monetary and nonmonetary in nature (Lee & Kotler, 2011, pg. 268). ART is a priceless commodity for treating HIV and prevention as treatment in discordant couples. As previously described, access issues related to price should not be an issue in South African given the government provides ART for free or very low cost due to price

negotiations, subsidies and donations. Inexpensive items such as male and female condoms should be provided for free or low cost at CHTC, clinics and pharmacies. CHTC must be affordable, and ideally free, given it's the key entry point for HIV treatment and prevention for discordant couples. Other costs such as transportation to CHTC and clinics for ART and time off from work can be mitigated by offering subsidized transportation tickets or vouchers and implementing policies which allow penalty-free time off from work (SANAC, 2011). Non-monetary costs are more intangible, e.g., time and discomfort, are part of the previously described barriers influencing decisions (Lee & Kotler, 2011). If effective CHTC can be leveraged to overcome barriers to testing and disclosure, many of the intangible costs, e.g., psychological and physical threats, can be minimized.

Programs can also offer incentives to encourage adoption and adherence of behaviors. A possible incentive is the use of conditional cash transfers for various HIV prevention behaviors if the uninfected partner in the couple remains uninfected. This type of strategy has been used to encourage females, to stay HIV negative by adopting various behaviors (UNAIDS, 2013; SANAC, 2011). Another potential incentive is tax breaks for HIV prevention efforts for discordant couples. Although originally proposed to increase marriage rates in South Africa, the concept may be relevant in this setting. These incentives provide benefit by encouraging HIV prevention as well as providing social structural support (SANAC, 2011). However, these incentives need to be carefully considered given gender inequality issues which often exist within couples and the need to protect human rights issues regarding testing (Gay et al., 2012).

Place Marketing Strategy

Lee & Kotler define the place marketing component as "where and when the target audience will perform the desired behavior, acquire any related goods, and receive any

associated services" (2011, pg. 291). Place marketing strategies should focus on making locations: closer, with extended hours, the point of decision making, where people feel more at ease, channels for overcome psychological and physical barriers or perhaps familiar distribution channels (Lee & Kotler, 2011).

The CHTC serves as the "point of decision making," a springboard for educating couples about discordance and the need for HIV testing as well as guiding couples to engage in the other recommendations of concerning condom use and how ART can treat and prevent transmission to the uninfected partner. For these reasons, the place marketing strategy is especially critical for eliminating CHTC related barriers (Kelley et al., 2011).

Some CHTC can likely be conducted using existing clinics and prevention programs but with trained counselors adept at working with couples (Kelley et al., 2011). To overcome logistic issues, clinics and programs should offer extended hours to circumvent the couples' work and life commitments (Katz et al., 2009). Incorporating CHTC as part of existing services may facilitate normalizing CHTC and overcoming fear of joint testing (Kelley et al., 2011). Other channels for testing include partnering with community based organizations (CBO) and faith based organizations (FBO) to deploy program counselors who can utilize these facilities and coordinate with their members and activities (CDC, 2012). CBOs and FBOs are important channels of support as they will facilitate the dialogue about HIV in a non-clinical setting.

Another potential place to encourage CHTC is in the couples' homes via mobile testing sites which travel door-to-door through community targeted CHTC (Kelley et al., 2011). Home-based CHTC can be critical for those in rural settings where transportation and time away from work or family is a barrier (Gay et al., 2012). Home-based CHTC may also be a good option given some communities may have limited resources and are unable to set up permanent

facilities or staff. Moreover, the stigma, fear and discrimination often associated with HIV may make in home testing more attractive due to privacy issues (Wong, 2013).

Another reasonable access channel for CHTC is the workplace through partnership with highly trained counselors. The Siyazi Project is one such example in successful practice at 135 sites via a partnership supported by Jhpeigo, the US CDC, South Africa, and various private and public partnerships, resulting in 60,000 South Africans receiving HCT services at their workplace (Jhpeigo Corp, 2013). This project encourages companies to include HCT for employees and their families as part of routine wellness programs. This type of investment can enhance employee health, productivity and overall welfare and perhaps could be modified to target couples. Importantly, this type of counseling helps decrease stigma and encourages workers to "test, know and plan your life" (Jhpiego Corp., 2013). Finally, this project links individuals and their partners to testing, counseling and HIV support groups.

CHTC will be a viable place for couples to access condoms as will clinics and pharmacies. At distribution sites, condoms should be placed in easily accessible locations with promotional signage emphasizing condoms are for long term couples. Beyond CHTC, these couples will need convenient and affordable places to access their provision of ART. South Africa is already working on new policies and infrastructure to increase access to HIV care services at local health clinics versus requiring patients (and their partners) to travel to inconvenient places (Beaubian, 2013). Programs may consider partnering with CBOs to serve as a place for distribution of ART and other HIV-related care (Kennedy et al., 2010).

Promotion Marketing Strategy

The promotional marketing component is defined as "the persuasive communications designed and delivered to inspire [the] target audience to action," or more specifically the tools

for highlighting the products and services benefits and incentive and show to access them (Lee & Kotler, 2011, pg. 319). The promotional messages associated with these types of collective recommendations should communicate standardized but targeted messages which seek to increase couples perceived threat of HIV, as well as the "how" and "where" of accessing CHTC. Messages should explain the significance of discordance and the implications of treatment of as prevention strategies to maintain their partner's uninfected status (Kelley et al., 2011). Moreover, promotional messaging should be geared towards increasing the perceived benefits of CHTC and keeping both partners healthy with ART. Essential to this messaging is highlighting how the other marketing strategies of product, price and place can decrease barriers to accessing these services. Although the collective recommendations previously described are reasonable in theory, these couples may be facing tremendous stigma and years of unchartered territory; thus it is essential that the couples perceive that the benefits outweigh their barriers so they can adopt these behaviors in their real lives.

In terms of messengers, CBOs and FBOs can supplement the work of program messengers by acting as a non-clinical voice in favor of these collective recommendations. The CBOs and FBOs maintain a unique position by emphasizing benefits even in the reality of these couples' current settings. CBOs and FBOs can also effectively address misinformation and beliefs specific to each community context and reduce stigma. As trusted entities, these leaders can guide couples to places where they can access easy to understand facts about HIV and emphasize the prevention impact of CHTC, condoms and ART (Kelley et al., 2011).

Mass and social media, e.g., advertisements via radio, text messages, and billboards, can be harnessed to distribute information but also acknowledge the presence and relevance of discordant couples, emphasize CHTC, reduce stigma of HIV and encourage condom use and

ART for treatment and treatment as prevention (Kelley et al., 2011). Finally, it is critical to equally target men and women given their societal roles, gender issues, need for collective buy-in and for normalization in discussing these issues (Harrison et al., 2006; Katz et al., 2009).

Next Steps

The preliminary social marketing outline presented here provides examples of possible product, price, place and promotion strategies to encourage heterosexual discordant couples' uptake and adherence to a treatment as prevention program. However, it will be critical to develop and deploy a comprehensive social marketing plan which strategically links the marketing mix elements rather than utilizing each component as distinct strategies (Lee & Kotler, 2011). In order to accomplish this goal, detailed formative research should be conducted which is inclusive of the diverse geographic, socioeconomic and cultural groups comprising the larger target audience of discordant couples. Without such formative research and incorporation of tailored marketing mixes for various groups, there is a high risk of developing a social marketing campaign which caters to what developers believe the audience values and needs instead of identifying what program facets best serve this subpopulation (Lee & Kotler, 2011).